

**REMARKS**

Applicants have amended claims 1, 3-8, 10-11, 13-16 and 18 and have canceled claim 2 without prejudice to or disclaimer of the subject matter contained therein. As such, claims 1, 3-16 and 18-20 are currently pending in the present application.

No new matter has been introduced to the claims within the meaning of 35 U.S.C. §132. Accordingly, entry of the amendments is respectfully requested and further and favorable consideration is earnestly solicited in view of the following remarks.

**1. Rejection of Claims 1-16 and 18-20 Under 35 U.S.C. §112, 1<sup>st</sup> Paragraph**

The Official Action states that claims 1-16 and 18-20 are rejected under 35 U.S.C. §112, 1<sup>st</sup> paragraph because the specification “does not reasonably provide enablement for making solvates.”

First, Applicants respectfully note that claim 2 has been canceled without prejudice to or disclaimer of the subject matter contained therein, rendering the basis for this rejection moot.

With regards to presently pending claims 1, 3-16 and 18-20, Applicants respectfully traverse this rejection. However, in order to advance prosecution, and without acquiescence to the rejection or disclaimer to the subject matter recited or amended, Applicants have amended the rejected claims deleting the rejected subject matter. In particular, Applicants have deleted any reference to solvates of the claimed compounds.

Applicants submit that this amendment renders this rejection moot. As such, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of pending claims 1, 3-16 and 18-20.

**2. Rejection of Claims 1-16, 18 and 20 under 35 U.S.C. §103(a)**

The Official Action states that claims 1-16, 18 and 20 are rejected under 35 U.S.C. 103(a) as being obvious over Magee et al. (US Application Publication 2002/0111495).

As the basis of the rejection, the Official Action states in relevant part:

Magee et al. teaches the use of selective PDE4 inhibitors for improved therapeutic treatment of a number of inflammatory, respiratory and allergic diseases including chronic rhinitis. Magee et al. further teaches that the present compounds can be used together in combination with one or more therapeutic agents including antihistaminic H2 receptor antagonists such as azelastine, the steroid ciclesonide and with pharmaceutically [sic] carriers. The compositions of Magee et al. can be administered to humans. Magee et al. also teaches the route of administration that can critically affect bioavailability, solubility of the active agents and rapid absorption. By carriers, Magee et al. teaches addition of acceptable diluents, adjuvants, vehicles [sic] viscosity modifiers and other agents known to the artisan for providing favorable properties to the final pharmaceutical composition including water as a solvent, salts such as sodium chloride for isotonic properties (i.e. osmotic pressure-controlling agent; instant claim 7), cellulose-based substances such as sodium carboxymethylcellulose, polyethylene glycol as a wetting agent, polyethylene polyoxypropylene block polymer as a surfactant, emollients, humectants such as glycerin (instant claim 13), surfactants and sugars such as glucose. Magee et al. further teaches the composition for intranasal application.

Magee et al. does not particularly teach a composition with a particular osmotic pressure or a composition containing microcrystalline cellulose as solid particles in an aqueous medium.

However, Magee et al. does teach the inclusion of water-low soluble substance such as cellulose derivatives which encompasses all

substances containing cellulose including microcrystalline cellulose [(MCC)] which are solid particles before addition to the pharmaceutical composition. Moreover, Magee et al. teaches the use of viscosity modifiers and given that [MCC] is a well-known viscosity modifier, one of ordinary skill would readily add such compound as solid particles as to obtain the desired product with the desired osmotic pressure. Additionally, Magee et al. teaches the addition of osmotic pressure controlling agents including glucose and sodium chloride. Consequently, these agents would necessarily affect the osmotic pressure of the composition due to their isotonization properties. Thus, to acquire the desired osmotic pressure for enhancing the bioavailability of the active ingredients as suggested by Magee et al., one of ordinary skill would be motivated to vary the concentration of the osmotic pressure controlling agents in a particular form of the composition.

### **RESPONSE**

First, Applicants respectfully note that claim 2 has been canceled without prejudice to or disclaimer of the subject matter contained therein, rendering the basis for this rejection moot.

With regards to presently pending claims 1, 3-16, 18 and 20, Applicants respectfully traverse this rejection. The cited references do not establish a *prima facie* case of obviousness against the presently pending claims.

To establish a *prima facie* case of obviousness, the PTO must satisfy three requirements. First, as the U.S. Supreme Court recently held in KSR International Co. v. Teleflex Inc. et al., Slip Opinion No. 04-1350, 550 U.S. \_\_\_\_ (April 30, 2007), "a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions. ...it [may] be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether

there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. ...it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does... because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known.” (KSR, supra, slip opinion at 13-15). Second, the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. Amgen Inc. v. Chugai Pharm. Co., 18 USPQ 1016, 1023 (C.C.P.A 1970). Lastly, the prior art references must teach or suggest all the limitations of the claims. In re Wilson, 165 USPQ 494, 496 (C.C.P.A. 1970).

Applicants respectfully submit that the broadest independent claim, claim 1, has been amended to recite a pharmaceutical composition which “has an osmotic pressure of less than 290 mOsm”.

The Examiner has relied on the Magee et al. reference in the rejection of presently pending claims 1, 3-16, 18 and 20.

Applicants take issue with the Examiner's statement on page 11 of the Official Action that the Magee et al. reference “does not particularly teach a composition with a particular osmotic pressure...” Actually, while the Magee et al. reference does not expressly teach a specific numerical value for the osmotic pressure pharmaceutical compositions, it does teach isotonic compositions, i.e., compositions that are equal to 290mOsm. Particular reference is made to the last few sentences of paragraph [708] of

the Magee et al. reference which teach that the solutions of the invention may be formulated as isotonic solutions. By definition, an isotonic solution has an osmotic pressure of 290mOsm. Solely for evidence regarding how an isotonic solution is defined, Applicants have included herewith an article from the journal "Anesthesiology" entitled "Rebound swelling of Astroglial Cells Exposed to Hypertonic Mannitol [Laboratory Investigations]", Anesthesiology, Vol. 88(6), June 1998, pp. 1586-1591. Applicant has highlighted the relevant portion of this reference under the "Experimental Solutions" section.

In contrast, Applicants respectfully submit that the presently claimed invention is directed to a hypotonic composition, i.e. a composition with an osmotic pressure of less than 290 mOsm. Magee et al. contains absolutely no teaching regarding compositions that are hypotonic.

Applicants further note the Examiner's comment that "applicant is reminded that a prior art reference may 'render obvious' without disclosing a feature of the claimed invention, as long as that missing characteristic is necessarily present, or inherent, in the anticipating reference." Applicants respectfully submit that they are fully aware of the doctrine of inherency and respectfully submit that the Magee et al. does not expressly or inherently teach the presently claimed invention.

Further, Applicants respectfully submit that hypotonic solutions enhance the uptake of the active ingredient over those solutions that are simply isotonic. Magee et al. has absolutely no teaching in this regard.

In view of the disclosure contained in paragraph [0708], the Magee et al. reference neither expressly nor inherently renders the presently pending claims obvious

in view of its clear teaching of isotonic compositions. A person of ordinary skill in the art would not be motivated to alter the teaching contained in the Magee et al. reference to arrive at the presently pending claims directed to hypotonic compositions. In fact, a person of ordinary skill in the art would be taught away from preparing the present invention directed to hypotonic compositions.

Accordingly, the Examiner has failed to establish a *prima facie* case of obviousness against the presently pending claims because the cited reference fails to teach each and every element of the presently pending claims as required by In re Wilson. If the Examiner insists that a *prima facie* case of obviousness has been established, the Examiner must remove this rejection in view of the divergent teachings contained in the Magee et al. regarding isotonic compositions.

As such, the Examiner is respectfully requested to withdraw this rejection of presently pending claims 1, 3-16, 18 and 20.

### **3. Rejection of Claim 19 under 35 U.S.C. §103(a)**

The Official Action states that claim 19 is rejected under 35 U.S.C. 103(a) as being obvious over Magee et al. (US Application Publication 2002/0111495) in view of Calatayud et al. (US Patent No. 5,482,934)

### **RESPONSE**

Applicants respectfully traverse this rejection. The cited references do not establish a *prima facie* case of obviousness against the presently pending claim.

For the sake of brevity, Applicants' arguments regarding the Magee et al.

reference outlined in section 2 above are incorporated by reference in their entirety.

The Calatayud et al. reference does not remedy the deficient teachings of the Magee et al. reference. Calatayud et al. do not teach any particular osmotic pressure, much less the hypotonic compositions of the presently pending claims.

Accordingly, the Examiner has failed to establish a *prima facie* case of obviousness against the presently pending claim because the cited references fail to teach each and every element of the presently pending claims as required by In re Wilson. If the Examiner insists that a *prima facie* case of obviousness has been established, the Examiner must remove this rejection in view of the divergent teachings contained in the Magee et al. regarding isotonic compositions.

As such, the Examiner is respectfully requested to withdraw this rejection of presently pending claim 19.

#### **4. Rejection of Claims 1-16, 18 and 20 under 35 U.S.C. §103(a)**

The Official Action states that claims 1-16, 18 and 20 are rejected under 35 U.S.C. 103(a) as being obvious over Szelenyi et al. (WO01/22955-corresponding to US Patent No. 7,022,687) in view of Schmidt et al.

#### **RESPONSE**

Again, Applicants respectfully note that claim 2 has been canceled without prejudice to or disclaimer of the subject matter contained therein, rendering the basis for this rejection moot.

With regards to presently pending claims 1, 3-16, 18 and 20, Applicants

respectfully traverse this rejection. The cited references do not establish a *prima facie* case of obviousness against the presently pending claims.

Similar to the Magee et al. reference discussed above in section 2, the Szelenyl et al. reference teaches isotonic compositions and contains absolutely no teaching regarding the presently claimed hypotonic compositions. Particular reference is made to col. 4, lines 29-33 of the corresponding '687 US Patent to Szelenyl et al. This section of the reference discusses suitable excipients for making the formulations isotonic. As with the Magee et al. reference, Szelenyl et al. teach the ordinary skilled artisan away from making the presently claimed formulations hypotonic.

The Schmidt et al. reference does not remedy the deficient teachings of the Szelenyl et al. reference. Schmidt et al. do not teach any particular osmotic pressure, much less the hypotonic compositions of the presently pending claims.

Accordingly, the Examiner has failed to establish a *prima facie* case of obviousness against the presently pending claims because the cited references fail to teach each and every element of the presently pending claims as required by In re Wilson. If the Examiner insists that a *prima facie* case of obviousness has been established, the Examiner must remove this rejection in view of the divergent teachings contained in the cited Szelenyl et al. reference regarding isotonic compositions.

As such, the Examiner is respectfully requested to withdraw this rejection of presently pending claims 1, 3-16, 18 and 20.

#### **5. Rejection of Claim 19 under 35 U.S.C. §103(a)**

The Official Action states that claim 19 is rejected under 35 U.S.C. 103(a) as



being obvious over Szelenyl et al. in view of Schmidt et al. and further in view of Calatayud et al.

### **RESPONSE**

Applicants respectfully traverse this rejection. The cited references do not establish a *prima facie* case of obviousness against the presently pending claim.

For the sake of brevity, Applicants' arguments regarding the Szelenyl et al. and Schmidt et al. references outlined in section 4 above are incorporated by reference in their entirety.

The Calatayud et al. reference does not remedy the deficient teachings of these references. As stated above in section 3, Calatayud et al. do not teach any particular osmotic pressure, much less the hypotonic compositions of the presently pending claims.

Accordingly, the Examiner has failed to establish a *prima facie* case of obviousness against the presently pending claim because the cited references fail to teach each and every element of the presently pending claims as required by In re Wilson. If the Examiner insists that a *prima facie* case of obviousness has been established, the Examiner must remove this rejection in view of the divergent teachings contained in the Szelenyl et al. regarding isotonic compositions.

As such, the Examiner is respectfully requested to withdraw this rejection of presently pending claim 19.

**CONCLUSION**

Based upon the remarks, the presently claimed subject matter is believed to be patentably distinguishable over the prior art of record. The Examiner is therefore respectfully requested to reconsider and withdraw the outstanding rejections and allow all pending claims 1, 3-16 and 18-20. Favorable action with an early allowance of the claims pending in this application is earnestly solicited.

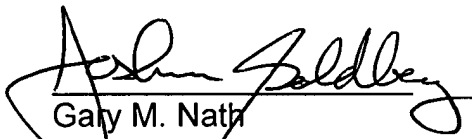
The Examiner is welcomed to telephone the undersigned attorney if he has any questions or comments. The Examiner is specifically authorized to charge any fee deficiency or credit any overpayment to Deposit Account No. 14-0112.

Respectfully submitted,

**THE NATH LAW GROUP**

Date: September 23, 2008

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